SUMMARY OF THE REJECTIONS

Claims 1-43 and 47-49 have been rejected under 35 USC 112, first paragraph

The basis of the rejection is believed to be fairly summarized as asserting as follows:

1) The specification enables practice of the invention for MRI methods only;
2) The specification does not enable a sensing method that detects the viability of implanted stems cells, progenitor cells, or differentiated cells;
3) Therefore the specification does not provide enablement commensurate in scope with the claims.

RESPONSE TO THE REJECTIONS

The Rejections Under 35 USC 112, first paragraph

There are a number of confusing and contradictory implications in the rejection. The indication that the specification is enabling for MRI methods only implies the generic functionality for the use of MRI imaging processes to effect the practice of the invention is enabled. On the other hand, the rejection asserts that the specification does not enable a method that detects the viability of stem cells, progenitor cells, and differentiated cells.

The problem with this rejection is the failure to appreciate that all of the various imaging or non-destructive testing methods described in the specification analyze for effects produced by the cells that are indicative of viability and do not measure 'viability' as a quantitative value itself. This is absolutely clear from the disclosure (under 35 USC 112, second paragraph) and is clearly enabled under 35 USC 112, first paragraph. Note the following specific disclosures:

a) "The invention additionally discloses an imaging system to monitor the metabolic status of the transplanted cells and their assimilation into their tissue transplant environment..." Page 5, lines 27-29;

b) "...the software program may operate in a manner that includes at least some of the following steps:..Measure the response of that field to an imaging technology (e.g., MR, fluoroscopy, sonogram, etc.)...Determine...components of the response that are associated with

specific readable components (e.g., taggants or natively responsive components, molecules or atoms...Introduce cells into the field. Identifying at least some readable components introduced to the field by introduction of the cells. Comparing concentrations and/or the change in the range...Observing concentrations of change in the range of presence of readable components. Qualitatively and/or quantitatively determining changes and/or rates of changes and/or locations of changes..." (Page 7, line 20-page 8, line 13).

c) "According to methods of the invention, cell viability may be assessed by monitoring the presence of anisotropic water diffusion. (Page 22, lines 18-20). Furthermore,...cell viability may also be assessed by monitoring the increases in local tissue density by measuring the water proton diffusion in the local tissue. (Page 22, lines 22-26).

d) "In another embodiment of the invention, the viability and functional assimilation of the implanted cells may be assessed by monitoring changes in the resting membrane potential of cells in the cell implant." (Page 23, lines 9-11).

e) "In a further embodiment of the invention, cell viability may also be assessed by measuring changes in electrical impedance in the region of the cell implant." (Page 23, lines 20-24).

f) "In a preferred embodiment of the invention, the development of cells into tissues will alter the inherent cellular luminescence, which is monitored by a local optical probe or camera introduced by an image-guided catheter." (Page 26, lines 4-13).

g) "In a further embodiment of the method of the invention, cell viability may be assessed by measuring changes in local tissue temperature using, as one example, probes introduced by image-guided catheters..." (Page 26, lines 19-23).

h) Pages 12, line 13 – page 14, line 15 describes various methods and mechanisms by which cell viability can be determined.

i) Additionally, the specific contains extensive disclosure or methods of analyzing numerous different local properties that are determined by MRI technology (e.g., Pages 15, line 15 – page 17, line 9; page 17, line 16 – page 18, line 3; page 18, line 19 – page 21, line 1; page 22, line 9 – page 23, line 19; page 24, line 6 – page 26, line 3; page 27, line 6 – page 28, line 8).

It is absolutely clear that specification provides a clear statement of measuring properties that are related to, quantifiable to, or quantitative to the viability of implanted cells in a patient. Different imaging methods are described and enabled (e.g., MRI, sonogram, fluoroscopy, optical fiber, catheter, etc.), different measuring methods are described and enabled (thermal measurements, electrical methods, etc.), and many different properties that can be measured by MRI are described an enabled. The specification therefore is clearly enabling of both various and numerous methods (and enablement is not limited to only MRI systems). The specification is also clearly enabling of various and numerous different properties that may be the basis of quantitative or qualitative measurement to provide a determination of viability of cell implantation. Applicants have therefore made a clear, extensive and enabling disclosure consistent with the requirements of 35 USC 112, first paragraph with respect to the breadth of the invention as claimed.

The rejection under 35 USC 112, first paragraph states, in effect that:

1) The specification enables practice of the invention for MRI methods only; **This has been clearly contradicted and overwhelmed by the cited portions of the specification where fluoroscopy, sonogram, resistance, optical fiber, thermal measurements and other methods have been disclosed and enabled.**
2) The specification does not enable a sensing method that detects the viability of implanted stems cells, progenitor cells, or differentiated cells; **This assertion has been contradicted and overwhelmed by the cited disclosure wherein specific measurements of specific properties have been specified and enabled to show viability, and both methodology and instrumentality have been described to effect this method.**

3) Therefore the specification does not provide enablement commensurate in scope with the claims. **Not only is this assumption in error based upon the review of the nature and extent of the disclosure, but the basis for challenging the disclosure is legally inadequate and insufficient as a matter of law.**

With regard to the third argument given directly above, it is to be noted that it is a fundamental requirement of the US PTO to establish and support any rejection based upon 35 USC 112, first paragraph with scientific reasoning and analysis of specific facts as to why a specification is not enablement. For example:

> "A threshold issue is whether the PTO met its burden of proof in calling into question the enablement of appellant's disclosure. This burden required that the PTO advance acceptable reasoning inconsistent with enablement.." *In re Strahilevitz*, (1982 C.C.P.A.) 212 U.S.P.Q. 561.

The rejection has not advanced any scientific reasoning why a process reasonably within the scope of the claims as drafted is not enabled. Rather, the specification merely says MRI is enabled, but that "...methods of indicting viability of 'implanted cells, progenitor cells, or differentiated cells' [have]...very limited guidance within the specification as to how this is accomplished. The claimed methods (referring to the broadest claim) require a 'sensing' function of cells within a region of a patient." Contrary to the subsequent misappropriation of language attempting to limit the application to MRI, the quoted language and portions of the specification cited above clearly provides enablement to one skilled in the art that is commensurate with the scope of the claims. It must be remembered that the legal issue of enablement is to be viewed in the light of one ordinarily skilled in the art.

> "Claims are addressed to the person of average skill in the particular art. Compliance with 112 must be adjudged from that perspective, not in a vacuum. It is always possible to theorize some combination of circumstances which would render a claimed composition or method inoperative, but the art-skilled would assuredly not choose such a combination. (*Ex parte Cole, Howarth and Reading*, (PTO Bd. Of Pat. Int. and App.) 233 USPQ 94.

Viewed from the legally required perspective, it is clear both that the PTO has not met even a threshold burden of establishing a *prima facie* case of lack of enablement, and has not given appropriate value to the scope and detail of the specification with respect to the breadth of the invention as viewed and understood by one ordinarily skilled in the art. The rejection is clearly in error and must be withdrawn.

It is also to be noted that some of the claims that have been rejected as lacking enablement recite MRI specifically as the method of imaging (claim 2 and every claim dependent therefore), and that other claims dependent therefrom recite specific methods used, specific properties used, and other limiting characteristics that are clearly enabled by the specification. The rejection is therefore completely inappropriate to such claims, such as, but not limited to, claims 2, 6, 8-9, 11-12, 14-16, 18, 21 and 23-24.

Applicants believe that the application and claims are now in proper order and in condition for allowance. Please direct any inquiries to the undersigned attorney at (952) 832-9090.

Respectfully submitted,

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